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YOUNG & THOMPSON			DOE, SHANTA G	
209 Madison Street			ART UNIT	
Suite 500			PAPER NUMBER	
Alexandria, VA 22314			1774	
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

DocketingDept@young-thompson.com

<b>Office Action Summary</b>	<b>Application No.</b> 10/590,348	<b>Applicant(s)</b> DE CRECY, EUDES FRANCOIS	
	<b>Examiner</b> SHANTA G. DOE	<b>Art Unit</b> 1774	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 23 August 2006.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 18-79 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 18-79 is/are rejected.
- 7) ☒ Claim(s) 47-53 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 23 August 2006 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

### ***Specification***

1. The disclosure is objected to because of the following informalities: The disclosure fails to provide antecedent basis/ support for the tube being transparent and/ or translucent as is claimed in claims 22, 38, 39, and 74.

Appropriate correction is required.

### ***Drawings***

1. The drawings are objected to under 37 CFR 1.83(a). The drawings must show every feature of the invention specified in the claims. Therefore, the stirring bar as is claimed in claims 27, 44, and 63, the pressure regulator as is claimed in claim 59, and the pH indicator as is claimed in claims 21, 41 and 60, must be shown or the feature(s) canceled from the claim(s). No new matter should be entered.

Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional

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replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

### ***Double Patenting***

2. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

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A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

3. Claims 18-29 and 35-44 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, 6-10, 12 and 13 of copending Application No. 11/508286. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the current application are anticipated by the claims of the copending Application No. 11/508286.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

4. Claims 54-79 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, 6-13, 16-21, and 26-36 of copending Application No. 11/508286. Although the conflicting claims are not identical, they are not patentably distinct from each

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other because the claims of the current application are anticipated by the claims of the copending Application No. 11/508286.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

### ***Claim Objections***

5. Claim 19 is objected to because of the following informalities: claim 19 does not further limit the device of claim 18 because claim 18 already states that the tube is flexible. Appropriate correction is required.

6. Claim 29 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only (the examiner is unsure whether "1-c" reads 1 dash c or 1 through c). See MPEP § 608.01(n).

### ***Claim Rejections - 35 USC § 112***

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 20,26, 29, 30-34, and 46-53 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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9. Regarding claim 20, the phrase "for example" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

10. Regarding claim 26, the phrase "any known method" renders the claim indefinite because it is unclear what exactly any known method entails.

11. Regarding claim 29, this claim is indefinite because the claim contains the limitation stating the tube can be tilted ...to remove air through the function described in claim 1-c. There is insufficient antecedent basis for "the functions". Additionally, there is no claim labeled claim 1-c which discusses the said functions.

12. Claims 30-34 recite the limitation "the described growth chamber". There is insufficient antecedent basis for this limitation in the claim.

13. Claim 46 recites the limitation "the second portion" There is insufficient antecedent basis for this limitation in the claim; However, there is antecedent basis for "the second region".

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14. Claim 47-53 recites the limitation "said device" There is insufficient antecedent basis for this limitation in the claim. However, the examiner believes "said device" should be replaced with "said method".

***Claim Rejections - 35 USC § 102***

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. Claims 18, 19, 23, 25, 26, 28, 29, 35, 36, 40, 42, 43, 45, 54-56, 61, 64-67, 69, 70-72, 77 and 78 are rejected under 35 U.S.C. 102(b) as being anticipated by Okazaki et al (JP 03-030665).

Regarding claim 18, Okazaki discloses a device that increases the rate of reproduction (see fig 1) comprising: a flexible sterile tube (1) containing culture medium; a system of clamps (2), each capable of open and closed positions, the clamps being positioned so as to be able to divide the tubing into separate regions containing spent culture (cultured fermenter (6)), growing culture (new fermenter (7)), and fresh growth medium (unused fermenter), and a means of moving the clamps and the tubing such that a portion of the growth chamber and the associated culture can be clamped off and separated from the growth chamber, and such that a portion of fresh tubing containing unused medium can



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be joined with a portion of the culture and associated medium already present in the growth, wherein each of the clamps does not move with respect to the tube when said clamp is in the closed position (see fig 1 and 2, and entire document).

Regarding claim 19, Okazaki discloses the device according to claim 18, wherein the tubing is flexible to allow clamping and segregation into separated chamber (see fig 1 and 2). Additionally, this claim does not further limit the device of claim 18 structurally.

Regarding claim 23, Okazaki discloses the device according to claim 18, wherein the growth chamber tubing and associated media and culture can be depressurized or over pressurized relative to ambient atmosphere as necessitated by experimental requirements (this claim does not further limit the device of claim 18 structurally, this claim appears to be an intended use of the claimed invention) (see fig 1 and 2, and entire document).

Regarding claim 25, Okazaki discloses the device according to claim 18, wherein the growth chamber tubing and associated media and culture can be heated or cooled as appropriate for experiment conditions (this claim does not further limit the device of claim 18 structurally; this claim appears to be an intended use of the claimed invention) (see fig 1 and 2, and entire document).

Regarding claim 26 Okazaki discloses the device according to claim 18, wherein

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the growth chamber tubing and associated media and culture can be kept motionless or agitated by any already known method (this claim does not further limit the device of claim 18 structurally, this claim appears to be an intended use of the applicant claimed invention) (see fig 1 and 2, and entire document).

Regarding claim 28, Okazaki discloses the device according to claim 18 wherein regions of the tubing can be confined in a specific and controlled atmospheric area to control gas exchange dynamics (this claim does not further limit the device of claim 18 structurally, this claim appears to be an intended use of the applicant claimed invention) (see fig 1 and 2, and entire document).

Regarding claim 29, Okazaki discloses the device according to claim 18 wherein the growth chamber tubing and associated media and the culture can be tilted either downward to remove aggregated cells, or upward to remove air through the function described in claim 1-c (this claim does not further limit the device of claim 18 structurally, this claim appears to be an intended use of the applicant claimed invention) (see fig 1 and 2, and entire document).

Regarding claim 35, Okazaki discloses a device that increases the rate of reproduction (through increased speed of reproduction and/or increased reproductive yield) of living cells in suspension or of any culturable organisms through the process of natural selection, said device comprising:  
a continuous length of flexible, sterile tubing (called flexible tube 1);

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a system of clamps (called cock 2) positioned at points along a section of the tubing, each of the clamps being positioned and arranged so as to be able to controllably pinch the tubing by putting said clamp into a closed position in which the tubing is divided into separate regions on respective sides of said clamp (see fig 1 and 2), the separate regions on respective sides of said clamp being merged back into a single region when said clamp is returned to an open position (see fig 1 and 2, and entire document). The phrase “wherein the clamps and tubing are arranged so that the tubing is clamped at first through fourth points along the tubing, defining first through third regions downstream of the first through third points, respectively; and wherein a volume of the second region delimited by said points two and three is greater than a volume of the first and third regions wherein the system of clamps is constructed so that, in a repeating pattern, the tubing is clamped upstream of the first point, the tubing is clamped at a point between the second and third points, and the second point is returned to the open position, thereby subdividing the second region into an upstream portion and a downstream portion, merging the first region and the upstream portion, and thereby defining new first through fourth points and first through third regions” appear to be an intended use of the applicant’s claimed invention which does not further limited the claim structurally. Additionally it appears the device as disclosed by the prior art would be capable of such intended use.

Regarding claim 36, Okazaki discloses the device according to claim 35, wherein

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the tubing is gas permeable (see page 3 of the English translation of the spec. paragraph 4)

Regarding claim 40, Okazaki discloses the device according to claim 35, wherein contents of the tubing in the second region can be controllably depressurized or over pressurized relative to ambient atmosphere (this claim does not further limit the device of claim 18 structurally, this claim appears to be an intended use of the applicant claimed invention ) (see entire document).

Regarding claim 42, Okazaki the device according to claim 35, further comprising a heating and cooling device that can control a temperature of contents of the tubing (see page 4 of the English translation of the spec. paragraph 4).

Regarding claim 43, Okazaki discloses the device according to claim 35, further comprising an agitator (stirring mechanism) (see fig 2; page 4 of the English translation paragraph 4).

Regarding claim 45, Okazaki discloses the device according to claim 35, wherein regions of the tubing can be confined in a specific and controlled atmospheric area to control gas exchange dynamics ( see fig 2 (incubator) ; entire document , specifically page 4).

Regarding claim 54, Okazaki discloses a device for growing living cells in a

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continuous manner, comprising: flexible tubing containing (flexible tube 1) culture medium; and a system of clamps (2), each capable of open and closed positions, the clamps (2) being positioned so as to be able to divide the tubing into:

i) an upstream region (unused fermenter) containing unused culture medium; ii) a downstream region (cultured fermenter) containing spent culture medium; and iii) a growth chamber (called new fermenter) region for growing said cells disposed between the upstream and downstream regions; wherein the system of clamps is constructed and arranged to open and close so as to clamp off and define the growth chamber region of the tubing between the upstream and downstream regions of the tubing, and to cyclically redefine the growth chamber region of the tubing so that a first portion of the previously defined growth chamber region becomes a portion of the downstream region of the tubing, and a portion of the previously defined upstream region of the tubing becomes a portion of the growth chamber region of the tubing(see fig 1 and 2, and entire document).

Regarding claim 55, Okazaki discloses the device according to claim 54, wherein the system of clamps is structured and arranged so that each of the clamps does not move with respect to the tubing when said clamp is in the closed position (see fig 1 and entire document).

Regarding claim 56, Okazaki discloses the device according to claim 54, wherein

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the tubing is gas permeable (see page 3 of the English translation of the spec. paragraph 4)

Regarding claim 61, Okazaki discloses the device according to claim 54, further comprising a temperature regulator constructed to control the temperature of the growth chamber region of the tubing (see fig 2 (incubator); entire document, specifically page 4).

Regarding claim 64, Okazaki discloses the device according to claim 54, wherein said growth chamber region comprises one or more growth chambers containing culture medium (see fig 1 (the new fermenter contains one growth chamber)).

Regarding claim 65, Okazaki discloses a method for growing cells in continuous manner, comprising: a) providing flexible tubing (1) and a system of clamps (2), each of the clamps being capable of open and closed positions, the clamps being positioned so as to be able to divide the tubing into: i) an upstream region containing unused culture medium (unused fermenter); ii) a downstream region containing spent culture medium (cultured fermenter); and iii) a growth chamber region (new fermenter) for growing (see fig 1 and 2) said cells disposed between the upstream and downstream regions; and b) closing selected ones of the clamps on the tubing to define the growth chamber region of the tubing between the upstream and downstream regions of the tubing, and introducing viable cells

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(implantation of culture) into the growth chamber region (see fig 1 and 2); c) cyclically closing and opening selected ones of the clamps to redefine the growth chamber region of the tubing so that a first portion of the previously defined growth chamber region becomes a portion of the downstream region of the tubing, and a portion of the previously defined upstream region of the tubing becomes a portion of the growth chamber region of the tubing; and d) repeating step c) until a sufficient amount of cells has been grown (see entire document).

Regarding claim 66, Okazaki discloses the method according to claim 65, comprising the further step of withdrawing a sample of living cells from said culture medium from said downstream region (ports 3 can be used for the occasional recovery of culture, see page 4 paragraph 4 lines 1-3) (see fig 3 & 4; page 4 paragraph 4 lines 1-3).

Regarding claim 67, Okazaki discloses the method according to claim 65, further comprising isolating said living cells from said downstream region (ports 3 can be used for the occasional recovery of culture, see page 4 paragraph 4 lines 1-3) (see entire document).

Regarding claim 69, Okazaki discloses the method according to claim 65, wherein said growth chamber region (called new fermenter) comprises one or

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more growth chambers containing culture medium (see fig 1 and 2).

Regarding claim 70, Okazaki discloses the method according to claim 65, wherein one or more species of organism are grown in said growth chambers (see entire document).

Regarding claim 71, Okazaki the method according to claim 65, wherein the sufficient amount of cells of step d) is defined as a pre-determined density level of the cells (this limitation seem to be inherent from what is taught in Okazaki)(see entire document especially page 4) .

Regarding claim 72, Okazaki discloses the method according to claim 65, wherein the tubing is gas permeable (see page 3 of the English translation of the spec. paragraph 4).

Regarding claim 77, Okazaki discloses the method according to claim 65, further comprising regulating the temperature of the growth chamber region with a temperature regulator constructed to control the temperature of the growth chamber region of the tubing (see page 5 of English translation).

Regarding claim 78, Okazaki discloses the method according to claim 65, further comprising agitating the culture medium in the growth chamber region with an



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agitator (see fig 2 and page 5 of the English translation).

17. Claims 18, 19, 21-23, 25, 26, 28, 29, 35, 37, 38, 39, 40, 54, 55, 57 and 58 are rejected under 35 U.S.C. 102(b) as being anticipated by Bieri (CH552063).

Regarding claim 18, Bieri discloses a device that increases the rate of reproduction (see fig 3 and 4) comprising: a flexible sterile tube (3) (see fig 3 and 4) containing culture medium (1); a system of clamps (called pinchcock(6)), each capable of open and closed positions, the clamps being positioned so as to be able to divide the tubing into separate regions (see fig 3 and 4) containing spent culture, growing culture, and fresh growth medium, and a means of moving the clamps and the tubing such that a portion of the growth chamber and the associated culture can be clamped off and separated from the growth chamber, and such that a portion of fresh tubing containing unused medium can be joined with a portion of the culture and associated medium already present in the growth, wherein each of the clamps does not move with respect to the tube when said clamp is in the closed position (see fig 3 and 4, and entire document).

Regarding claim 19, Bieri discloses the device according to claim 18, wherein the tubing is flexible to allow clamping and segregation into separated chamber (see fig 3 and 4). Additionally, this claim does not further limit the device of claim 18 structurally.

Regarding claim 21, Bieri discloses the device according to claim 18, wherein the tubing is gas impermeable, to prevent gas exchange between the tubing and the outside environment, if the experiment demands anaerobiosis (see entire document).

Regarding claim 22, Bieri discloses the device according to claim 18, wherein the tubing is transparent or translucent, to allow the measurement of turbidity (see paragraph 5).

Regarding claim 23, Bieri discloses the device according to claim 18, wherein the growth chamber tubing and associated media and culture can be depressurized or over pressurized relative to ambient atmosphere as necessitated by experimental requirements (this claim does not further limit the device of claim 18 structurally; this claim appears to be an intended use of the claimed invention) (see fig 3 and 4, and entire document).

Regarding claim 25, Bieri discloses the device according to claim 18, wherein the growth chamber tubing and associated media and culture can be heated or cooled as appropriate for experiment conditions (this claim does not further limit the device of claim 18 structurally, this claim appears to be an intended use of the applicant claimed invention) (see fig 3 and 4, and entire document).

Regarding claim 26 Bieri discloses the device according to claim 18, wherein the growth chamber tubing and associated media and culture can be kept motionless or agitated by any already known method (this claim does not further limit the device of claim 18 structurally, this claim appears to be an intended use of the claimed invention) (see fig 3 and 4, and entire document).

Regarding claim 28, Bieri discloses the device according to claim 18 wherein regions of the tubing can be confined in a specific and controlled atmospheric area to control gas exchange dynamics (this claim does not further limit the device of claim 18 structurally, this claim appears to be an intended use of the claimed invention) (see fig 3 and 4, and entire document).

Regarding claim 29, Okazaki discloses the device according to claim 18 wherein the growth chamber tubing and associated media and the culture can be tilted either downward to remove aggregated cells, or upward to remove air through the function described in claim 1-c (this claim does not further limit the device of claim 18 structurally; this claim appears to be an intended use of the claimed invention) (see entire document).

Regarding claim 35, Bieri discloses a device that increases the rate of reproduction (through increased speed of reproduction and/or increased

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reproductive yield) of living cells in suspension or of any culturable organisms through the process of natural selection, said device comprising:

a continuous length of flexible, sterile tubing (tube (1), see fig 3 and 4);

a system of clamps (called pinchcock(6)) positioned at points along a section of the tubing, each of the clamps being positioned and arranged so as to be able to controllably pinch the tubing by putting said clamp into a closed position in which the tubing is divided into separate regions on respective sides of said clamp (see fig 3 and 4), the separate regions on respective sides of said clamp being merged back into a single region when said clamp is returned to an open position (see fig 3 and 4, and entire document) . The phrase “wherein the clamps and tubing are arranged so that the tubing is clamped at first through fourth points along the tubing, defining first through third regions downstream of the first through third points, respectively; and wherein a volume of the second region delimited by said points two and three is greater than a volume of the first and third regions wherein the system of clamps is constructed so that, in a repeating pattern, the tubing is clamped upstream of the first point, the tubing is clamped at a point between the second and third points, and the second point is returned to the open position, thereby subdividing the second region into an upstream portion and a downstream portion, merging the first region and the upstream portion, and thereby defining new first through fourth points and first through third regions” appear to be an intended use of the applicant’s claimed invention which does not further limited the claim structurally. Additionally it appears the device as disclosed by the prior art would be capable of such intended use.

Regarding claim 37, Bieri discloses the device according to claim 35, wherein the tubing is gas impermeable (see entire document).

Regarding claim 38, Bieri discloses the device according to claim 35, wherein the tubing is translucent (see paragraph 5).

Regarding claim 39, Bieri discloses the device according to claim 35, wherein the tubing is transparent (see paragraph 5).

Regarding claim 40, Bieri discloses the device according to claim 35, wherein contents of the tubing in the second region can be controllably depressurized or over pressurized relative to ambient atmosphere (this claim does not further limit the device of claim 18 structurally, this claim appears to be an intended use of the applicant claimed invention ) (see entire document).

Regarding claim 54, Bieri discloses a device for growing living cells in a continuous manner, comprising: flexible tubing containing (tube (3)) culture medium; and a system of clamps (pinchcock(6)), each capable of open and closed positions, the clamps (pinchcock(6)) being positioned so as to be able to divide the tubing into:

i) an upstream region containing unused culture medium (which would be

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capable of containing unused culture medium); ii) a downstream region containing spent culture medium (which would be capable of containing spent culture medium); and iii) a growth chamber region for growing said cells disposed between the upstream and downstream regions; wherein the system of clamps is constructed and arranged to open and close so as to clamp off and define the growth chamber region of the tubing between the upstream and downstream regions of the tubing, and to cyclically redefine the growth chamber region of the tubing so that a first portion of the previously defined growth chamber region becomes a portion of the downstream region of the tubing, and a portion of the previously defined upstream region of the tubing becomes a portion of the growth chamber region of the tubing (see fig 3 and 4, and entire document).

Regarding claim 55, Bieri discloses the device according to claim 54, wherein the system of clamps is structured and arranged so that each of the clamps does not move with respect to the tubing when said clamp is in the closed position (see fig 3, 4 and entire document).

Regarding claim 57, Bieri discloses the device according to claim 54, wherein the tubing is gas impermeable (see entire document).

Regarding claim 58, Bieri discloses the device according to claim 54, wherein the tubing is transparent or translucent, to permit a turbidity meter to determine the density of the culture (see paragraph 5).

***Claim Rejections - 35 USC § 103***

18. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

19. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

20. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

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21. Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over Okazaki et al (JP 03-030665) in view of Taiariol et al (US 5,017,490).

Regarding claim 20, Okazaki discloses the device according to claim 18 wherein the tubing is gas permeable (see page 3 of the English translation of the spec. paragraph 4). However, Okazaki fails to specifically disclose that the tube is made from silicon.

Taiariol et al (US 5,017,490) discloses that is known in the art to have a cell culturing device made of flexible silicon rubber tube (see Taiariol entire document, col. 4 lines 3-5).

In view of Taiariol, it would have been obvious to one having ordinary skill in the art at the time of the invention to have the tubing comprise primarily of silicon, since it has been held to be within the general skill of a worker in the art to select a known material on the basis of its suitability for the intended use as a matter of obvious design choice.

22. Claims 24, 41, 60 and 76 are rejected under 35 U.S.C. 103(a) as being unpatentable over Okazaki et al (JP 03-030665) or Bieri (CH552063) in view Doi et al (US 2004/0029265).

Regarding claims 24, 41, and 60 Okazaki or Bieri discloses the device according to claim 18 or 35 or 54. However Okazaki or Bieri fails to disclose that the tubing comprises a pH indicator.



Doi et al (US 2004/0029265) discloses that a pH meter (pH indicator) is used in conjunction with the tube bioreactor to monitor the pH (see Doi [0054]).

In view of Doi, it would have been obvious to one having ordinary skill in the art at the time of the invention to have the tube of Okazaki comprise a pH indicator in order to monitor the pH of the contents of the device to make sure an optimal culturing climate is maintained.

Regarding claim 76, Okazaki discloses the method according to claim 65, However Okazaki or Bieri fails to disclose further measuring a pH of the culture medium in the growth chamber region.

Doi et al (US 2004/0029265) discloses that a pH meter (pH indicator) is used in conjunction with the tube bioreactor to monitor the pH (see Doi [0054]).

In view of Doi, it would have been obvious to one having ordinary skill in the art at the time of the invention to further measure the pH of the culture medium in the growth chamber region in order to monitor the pH of the contents of the device to make sure an optimal culturing climate is maintained.

23. Claims 59 and 75 are rejected under 35 U.S.C. 103(a) as being unpatentable over Okazaki et al (JP 03-030665) or Bieri (CH552063) in view of Redikultsev (US 4,686,189).

Regarding claim 59, Okazaki or Bieri discloses the device according to claim 54. Okazaki or Bieri fails to disclose that the device of claim 54 wherein the device

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further comprises a pressure regulator constructed to change a pressure of the growth chamber portion of the tubing relative to ambient pressure.

Redikultsev (US 4,686,189) discloses a device for growing cells (bioreactor (1)) wherein the device comprises a pressure regulator (15) to regulate the pressure of the bioreactor (see Redikultsev page 4 lines 25 -45).

In view of Redikultsev, it would have been obvious to one having ordinary skill in the art at the time of the invention to have the device of Okazaki or Bieri further comprise a pressure regulator since Redikultsev states (page 4 lines 40-45) that such a modification would aid in maintaining the pressure within the device.

Regarding claim 75, Okazaki discloses the method according to claim 65. Okazaki fails to disclose that the method further comprises regulating the pressure of the growth chamber portion of the tubing relative to ambient.

Redikultsev (US 4,686,189) discloses a device for growing cells (bioreactor (1)) wherein the device comprises a pressure regulator (15) to regulate the pressure of the bioreactor (see Redikultsev page 4 lines 25 -45).

In view of Redikultsev, it would have been obvious to one having ordinary skill in the art at the time of the invention to have the method further comprise regulating the pressure of the growth chamber portion of the tubing relative to ambient since Redikultsev states (page 4 lines 40-45) that such a modification would aid in maintaining the appropriate pressure conditions within the device.

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24. Claims 22, 38, 39 and 58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Okazaki et al (JP 03-030665) in view Bieri (CH552063).

Regarding claims 22, 38, 39 and 58, Okazaki discloses the device according to claim 18, 35, or 54. The Okazaki fails to disclose the device of claims 18, 34 or 54 wherein the tubing is one of transparent and translucent to permit a turbidimeter to determine the density of the culture.

Bieri (CH552063) discloses a transparent and translucent tube (30) used for growing cell culture (see Bieri entire document).

In view of Bieri, it would have been obvious to one having ordinary skill in the art at the time of the invention to have the tube of the Okazaki reference be transparent and translucent since such a modification would allow for one to view and examine the content of the bioreactor.

25. Claims 27, 44, 63 and 79 are rejected under 35 U.S.C. 103(a) as being unpatentable over Okazaki et al (JP 03-030665) in view of Yunker et al (US 4,703,010).

Regarding claims 27, 44 and 63, Okazaki discloses the device according to claim 18 or 35 or 54, wherein the agitator comprises a magnetic rotor. Okazaki fails to disclose that the agitator comprises at least one stirring bar.

Yunker et al (US 4,703,010) discloses a bioreactor comprising stirring bar used to agitate or stir the content of the reactor (see Yunker entire document).

In view of Yunker, it would have been obvious to one having ordinary skill in the art at the time of the invention to have the device of Okazaki comprise a stirring bar as is taught by Yunker because the stirring bar is a functionally equivalent means known in the art for stirring/agitating the content of a reactor.

Regarding claim 79, Okazaki discloses the method according to claim 78.

Okazaki fails to disclose that the agitator comprises at least one stirring bar.

Yunker et al (US 4,703,010) discloses a bioreactor comprising stirring bar used to agitate or stir the content of the reactor (se Yunker entire document).

In view of Yunker, it would have been obvious to one having ordinary skill in the art at the time of the invention to have the device of Okazaki comprise a stirring bar as is taught by Yunker because the stirring bar is a functionally equivalent means known in the art for stirring/agitating the content of a reactor.

26. Claim 46 is rejected under 35 U.S.C. 103(a) as being unpatentable over Okazaki et al (JP 03-030665) or Bieri (CH552063) in view of Watanabe et al (US 5,071,760).

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Regarding claim 46, Okazaki or Bieri discloses the device according to claim 35.

The above references fail to disclose that the device further comprises a device to control tilting of the second portion of the tubing.

Watanabe et al (US 5,071,760) discloses a device for culturing/growing cells having a culture container whereby the device further comprise a tilting device (called rotation system/mechanism; see fig 6,8,22, and 25 ) (see Watanabe fig 6,8,22, and 25 and entire document).

In view of Watanabe, it would have been obvious to one having ordinary skill in the art at the time of the invention to have the device further comprise a device to tilt the culturing device of Okazaki or Bieri because such a modification would serve as an agitation tool to aid in mixing the contents of the culture container.

27. Claims 68 and 73 are rejected under 35 U.S.C. 103(a) as being unpatentable over Okazaki et al (JP 03-030665).

Regarding claim 68, Okazaki discloses the method according to claim 65 comprising culturing microorganisms or cells. Okazaki fails to specifically disclose that the cells being cultured are selected from the group consisting of Yeast, Bacteria, Archae, Eukaryotes, and Viruses.

However, it would have been obvious to one having ordinary skill in the art to culture any known microorganism or cell within the culturing method as disclosed by Okazaki.

Regarding claim 73, Okazaki discloses the method according to claim 65.

Okazaki fails to disclose that the tubing is gas impermeable.

However, it would have been obvious to one having ordinary skill in the art at the time of the invention to have the tubing of the culturing device be made of a gas impermeable material, since it has been held to be within the general skill of a worker in the art to select a known material on the basis of its suitability of the intended use as a matter of obvious design choice.

28. Claim 74 is rejected under 35 U.S.C. 103(a) as being unpatentable over Okazaki et al (JP 03-030665) in view of Bieri (CH552063) and Alarcon et al (US 6,537,772).

Regarding claim 74, Okazaki the method according to claim 71. Okazaki fails to disclose the method of claim 71 wherein the tubing is one of transparent and translucent, turbidimeter being used to determine the density level of the cells.

Bieri (CH552063) discloses a transparent and translucent tube (30) used for growing cell culture (see Bieri entire document).

Alarcon et al. (US 6,537,772) discloses that it is known in the art to use a turbidimeter to detect changes due to microbial growth (density of the cell) (see Alarcon abs)

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In view of Bieri and Alarcon, it would have been obvious to one having ordinary skill in the art at the time of the invention to have the tube of the Okazaki reference be transparent and translucent since such a modification would allow for one to view and examine the content of the bioreactor. Additionally, it would have been obvious to one having ordinary skill in the art at the time of the invention to further have a turbidimeter being used to determine the density level of the cells because such a modification would enable one to monitor the growth of microorganism in the growth chamber.

***Allowable Subject Matter***

29. Claims 47-53 would be allowable if rewritten or amended to overcome the rejection(s) under 35 U.S.C. 112, 2nd paragraph, set forth in this Office action.

30. The following is a statement of reasons for the indication of allowable subject matter:

Regarding claim 47 and its dependent claims, the prior art fails to disclose/fairly suggest a method that increases the rate of reproduction (through increased speed of reproduction and/or increased reproductive yield) of living cells in suspension or of any culturable organisms through the process of natural selection, wherein said method comprising steps of: providing a continuous length of flexible, sterile tubing and a system of clamps positioned at points

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along a section of the tubing, closing the clamps at first through fourth points along the tubing to define first through third regions downstream of the first through third points, respectively, wherein the volume of the second region is greater than a volume of the first and third regions; and allowing the culture to grow in the culture medium in the second region; and repeating a step that comprises clamping the tubing upstream of the first point, clamping the tubing at a point between the second and third points, and returning the second point to the open position, thereby subdividing the second region into an upstream portion and a downstream portion, merging the first region and the upstream portion, and thereby defining new first through fourth points and first through third regions.

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHANTA G. DOE whose telephone number is (571)270-3152. The examiner can normally be reached on Mon-Fri 8am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Walter Griffin can be reached on 571-272-1447. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.



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SD

/Walter D. Griffin/  
Supervisory Patent Examiner, Art Unit 1774